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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/790,489 | 03/01/2004 | Keith Allan Freehauf | MER 03-017 | 9517 |

33928 7590 04/14/2008

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| EXAMINER | |
|---|---|
| SPIVACK, PHYLLIS G | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1614 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 04/14/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/790,489 | FREEHAUF, KEITH ALLAN | |
| | Examiner | Art Unit | |
| | Phyllis G. Spivack | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 4-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's Amendment filed January 7, 2008 is acknowledged. Claim 3 is canceled. Claims 1, 2 and 4-23 remain under consideration.

Applicant's arguments have been fully considered. Those rejections that are not herein reiterated are withdrawn. The following rejections constitute the only rejections applied to the present claims.

It was asserted in the last Office Action the instant specification claims the benefit of prior-filed U.S. Provisional Application No. 60/530939, filed December 19, 2003. Support for each concentration range of the recited ingredients, as well as the pH range recited in claim 13, was not found in the '939 application. As such, the earliest effective U.S. filing date of the instant application was determined to be March 1, 2004.

Applicant argues although the pH range is not specifically recited in the '939 application, it is clear that the earlier claimed stabilized feed premix formulations were prepared under the same pH, as both applications have identical preparation procedures. Applicant urges stability results for the claimed formulations are identical.

Claim 13 recites ranges for at least one avermectin compound; excipients, including various surfactants, waxes, antioxidants and carrier components; stabilizers and, optionally, at least one insect growth regulating compound. A comparison of Example 1 of each application shows the preparation procedures are not identical with respect to the "formulated antioxidant." Further, Table I in the "939 application and Table II in the present application are both drawn to a comparison of the stability of ivermectin at different degrees of temperature and relative humidity. These comparisons do not provide support for – and are not suggestive of – the concentration

ranges of each ingredient, as well as the pH range of component ( c), in the premix of claim 13.

Particularly in view of the criticality of the pH range, the earliest effective U.S. filing date of the instant application is still determined to be March 1, 2004.

Claims 1-23 were rejected under 35 U.S.C. 112, first paragraph, in the last Office Action, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention. The claims are directed to a premix for an animal feed that exhibits an extended shelf life, and methods thereto. It was asserted the specification does not reasonably provide enablement for the compositions and methods within the full scope of the claims.

Applicant argues the subject application provides methods for successful stabilization and extension of shelf life of the claimed formulations. Applicant urges a person skilled in the art can easily derive from the instant specification that the present invention can be applied to milbemycins and that other stabilizers can be used to decrease or to prevent the acid/base catalyzed decomposition of the active ingredient in the claimed formulation. A decomposition of milbemycins is hypothesized wherein Applicant urges maintaining pH between 4 and 6 in formulations containing milbemycins would decrease or prevent decomposition. Applicant additionally hypothesizes various stabilizers *can be used* to adjust the pH range. Applicant argues the breadth of the claims is not unduly broad as the method of extending the shelf life of premix formulations relates to compositions comprising avermectin or milbemycin derivatives

susceptible to acid/base decomposition, and stability depends on maintaining the pH between 4 and 6.

Applicant's arguments have been given careful consideration but are not found persuasive. The rejection of record of claims 1, 2 and 4-23 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification, is maintained for the reasons of record.

The invention is drawn to a combination composition intended to be used as a premix for an animal feed comprising a parasitically effective amount of at least one of the anthelmintics avermectin or milbemycin formulated with various pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles, stabilizers and, optionally, at least one insect growth-regulating compound, along with methods for extending the shelf life of a premix for an animal feed.

Applicant's arguments are primarily based on what *can be* used, *can be* applied, *can be* related, and *can be* achieved, with respect to any stabilizer and avermectin or milbemycin compounds. Applicant states Table II in the specification presents results that are intended to illustrate the general effect of the additional amount of stabilizer.

In fact, there is a single working example drawn to a comparison with and without citric acid (Table II on page 17) under defined storage conditions with respect to temperature and humidity over time (pages 18-20). No results are provided drawn specifically to any other premix formulations wherein a milbemycin or a different stabilizer is employed.

Thus, Applicant has failed to provide guidance as to other combinations that would reasonably be expected to demonstrate an extension of the shelf life of various avermectins and milbemycins. In view of the industrial problem that is recognized in the prior art concerning stability of such formulations, the disclosure is not commensurate in scope with the present claims. No direction is provided to distinguish among the various stabilizers that appear to be the most critical element in stabilization of the final product. Accordingly, one skilled in the art would have to test extensively the various pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles, stabilizers and, optionally, at least one insect growth-regulating compound to discover which particular combination in a premix for an animal feed exhibits an extended shelf-life. Undue experimentation would be required to practice the invention as it is claimed in its current scope. The instant claims do not comply with the enablement

requirements of 35 U.S.C. 112, first paragraph, since to practice the claimed invention would require a person of ordinary skill in the art to engage in undue experimentation with no assurance of success.

In the last Office Action claims 1-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Beuvry et al., U.S. Patent 5,824,653, in view of Katoh et al., U.S. Patent 4,939,166, Chabala et al., U.S. Patent 4,199,569, Sutherland et al., U.S. Patent 4,910,219, Freehauf et al., U.S. Patent 7,001,889, and Carson et al., U.S. Patent 6,548,478. It was asserted Beuvry teaches anthelmintic compositions comprising avermectins, milbemycins, or derivatives thereof, comprising surfactants and stabilizers.

See column 2, line 37. As required by instant claim 2, ivermectin, a semisynthetic derivative of avermectins is disclosed in column 2, line 39. Another avermectin, abamectin, is part of the formulation of Example 1, column 3. Further, the antioxidant, sodium metabisulfite, is encompassed in Example 1. The open language of the present claims allows for the inclusion of any number of additional active or inactive agents.

With respect to the requirements of the present claims for pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles and, optionally, insect growth-regulating compounds in animal feed compositions comprising avermectins and milbemycins:

Chabala teaches feed premixes comprising avermectins and milbemycins utilize carriers such as corn meal, citrus meal, fermentation residues, ground oyster shells, wheat shorts, molasses solubles, corn cob meal, bean mill feed, soy grits, dried grains and crushed limestone. See column 8, lines 11-21. Further, Sutherland teaches compositions for veterinary medicine comprising macrolides of formula II may be formulated to include the waxes glyceryl monostearate or coconut oil. See column 5, line 16. Katoh broadly teaches the inclusion of surfactants in a premix for an animal feed comprising macrolide compounds that are structurally analogous to avermectins and milbemycins. See column 10, lines 40-43, and column 14, lines 5-8. Carson teaches the inclusion of anhydrous citric acid in foodstuffs such as feed grain comprising macrolide antibiotics. See the Examples. As required by instant claim 13, the amount should be sufficient to provide a pH of from about 3.0 to about 7.0 in order to minimize the breakdown of the components of the mixture. See column 1, lines 51-

61, and column 2. Freehauf teaches the inclusion of avermectins and milbemycins in oral compositions intended for swine or equine administration, wherein pH stabilizers such as maleic acid or citric acid, antioxidants, such as sodium metabisulfite or ascorbic acid, and surfactants, such as hydrogenated castor oil, are further included.

Applicant argues Carson relates to the use of buffers for stabilizing a water suspension of virginiamycin, and not a solid formulation. With respect to the Freehauf document, Applicant further argues Freehauf relates to an oral veterinary paste consisting essentially of praziquantel and ivermectin. Applicant urges it is not obvious that the same stabilizers will decrease or prevent decomposition of avermectins or milbemycins since "the main ingredient is praziquantel." Applicant urges the present invention discloses solid materials as carrier vehicles, while Freehauf relates to a paste formulation comprising polar solvents.

Applicant's arguments have been given careful consideration but are not found persuasive. The rejection of record of claims 1, 2 and 4-23 under 35 U.S.C. 103(a) as being unpatentable over Beuvry et al., U.S. Patent 5,824,653, in view of Katoh et al., U.S. Patent 4,939,166, Chabala et al., U.S. Patent 4,199,569, Sutherland et al., U.S. Patent 4,910,219, Freehauf et al., U.S. Patent 7,001,889, and Carson et al., U.S. Patent 6,548,478, is maintained for the reasons of record.

Each of Carson's "preferred formulation" and Examples 1-3, columns 3 and 4, may be properly characterized as a "premix" in that each is a mixture that is preferably maintained as substantially anhydrous prior to forming a suspension, in order to minimize the breakdown of the components of the mixture. According to Carson, the

shelf life can be maximized. See lines 1-2, column 3. Thus Carson teaches a premix comprising stabilizers that are incorporated for the purpose of extending the shelf life of the veterinarian antibiotic formulation.

The present claims employ open (comprising) language. The premix of instant claim 1, and the method of extending the shelf life of a premix, are open to the inclusion of any number, and any type, of additional active or inactive agents. Further, a paste qualifies as a premix in that it is an oral composition intended for administration to warm-blooded animals or birds. The anthelmintics are dissolved in a solvent, but then they are dispersed in a carrier matrix which is a paste. The paste is formed by the addition of thickeners and opacifiers. See column 8 lines 13-27. Preferred ranges for pH are about 4 to about 6.5. The buffers contemplated to stabilize the formulations are recited in column 8, line 60, to column 9, line 1. The resultant oral veterinary paste is a soft solid. Freehauf teaches such pastes achieve a better bioavailability of anthelmintic agents than when the active agent is in suspension.

In view of the combined teachings of the prior art, one skilled in the veterinary art would have been motivated to prepare a premix for an animal feed comprising at least one avermectin or milbemycin in combination with a pharmaceutically acceptable surfactant, wax, antioxidant, stabilizer and carrier vehicle with a reasonable expectation of having an extended shelf-life. Such would have been obvious in the absence of evidence to the contrary because Carson teaches the inclusion of anhydrous citric acid in foodstuffs, such as feed grain comprising macrolide antibiotics, in amounts sufficient to provide a pH of from about 3.0 to about 7.0. The inclusion of anhydrous

citric acid in animal feed will minimize the breakdown of the components of the mixture and extend the shelf life of the product.

No claim is allowed.

Applicant's request for an interview is noted.

Applicant may contact the Examiner to establish an interview time and date.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The examiner can normally be reached on 10:30 AM-7 PM.

If attempts to reach the examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached on 571-272-

0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614

April 8, 2008